<u>Urine Concentration & Dilution</u>

Dr. Doaa Abou-Bakr

Ass. Prof. of Physiology

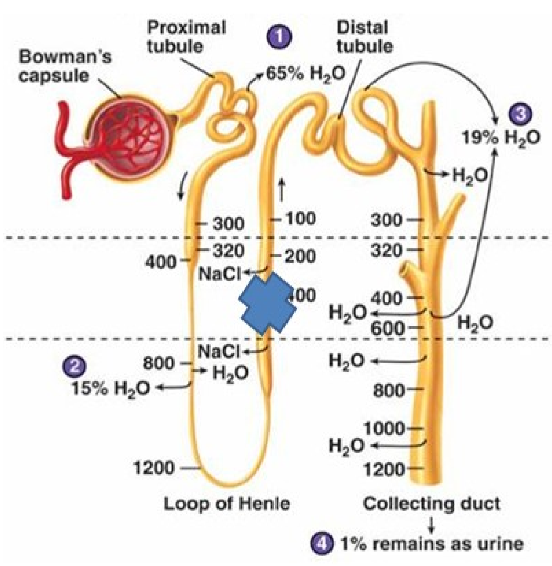
<u>ILOs:</u>

By the end of this lecture, you should be able to:

1. Mention mode of **handling** of water along nephron.
2. Discriminate **obligatory** and **facultative** water reabsorption.
3. Define the **countercurrent** system.
4. Describe the renal countercurrent system, its components and importance.
5. Explain the role of **loop of Henle** of juxta medullary nephrons in creating an osmotic gradient in the medullary interstitium (the countercurrent multiplication system).
6. Discuss the role of **vasa recta** as countercurrent exchanger in maintaining the hyperosmolarity of the medullary interstitium.
7. Explain how **urea** reabsorption contributes to the hyperosmotic renal medullary interstitium.
8. Describe the role of regional distribution of **renal blood flow** in creating hyperosmolarity of the medullary interstitium.
9. Explain how the kidneys produce **concentrated** or **diluted** urine.
10. Distinguish **water diuresis** from **osmotic diuresis**.

<u>Renal handling of water</u>

- All parts of the nephron is permeable to water except ascending limb of LH.
- It is reabsorbed passively by osmosis.



-GFR: 125 ml/min. So, daily **filtered** volume of water 125 X 60 X 24 = 180.000 ml/day = 180 L/day

-99.2-99.8 % of filtered water will be **reabsorbed** = 178.5-179.5 L/day

-0.2-0.8% of filtered water **pass into urine**. So, the urinary output: 0.5-1.5 L/day

<u>Obligatory reabsorption</u>: not under hormonal control:

-65% from PCT

-15% from descending limb of LH

Facultative reabsorption: under ADH control:
-5% from late DCT
-10% from cortical CD
-4.2-4.8% from medullary CD.
N.B: Daily urine output: 0.5-1.5 L/day.
Obligatory urine output is 500 ml that is to get rid of wastes.

Countercurrent System

Definition: Is a system where there are 2 currents flowing parallel, opposite and in close proximity to each other.

Renal countercurrent system

Aim: Urine Concentration
Components: 3 key players

a. Loop of Henle of Juxtamedullary nephrons
b. Vasa Recta
c. Medullary Collecting Ducts

Loop of Henle of Juxtamedullary nephrons (Countercurrent multiplier) Active system

It is countercurrent: as the flow of tubular fluid in the descending limb is parallel, opposite, adjacent to its flow in ascending limb

It is multiplier: as it causes the medullary interstitial osmolarity to be multiplied from cortex (300mOsm/L) to renal papillae (1200-1400 mOsm/L) by throwing NaCl out in the medullary interstitium.

Function: Creates graded medullary interstitium hyperosmolarity.

Mechanism:

<u>Thin ascending limb</u>: filtrate reach the thin ascending limb is hypertonic (1200 mOsm/L) as water is reabsorbed from the descending limb concentrating NaCl inside. So, NaCl diffuses passively to the medullary interstitium under concentration gradient.

<u>Thick ascending limb:</u> Actively transport NaCl into the medullary interstitium using Na^+-K^+- $2Cl^-$

Q: What solutes contribute to the osmotic gradient, and what mechanisms deposit these solutes in the interstitial fluid?

- solutes contribute to the osmotic gradient: **NaCl**, **Urea**

- mechanisms deposit these solutes in the interstitial fluid: **countercurrent multiplication,** a function of the loop of Henle, which deposits NaCl in the deeper regions of the kidney; and **urea recycling**, a function of the inner medullary collecting ducts, which deposits urea.

Mechanism of Countercurrent Multiplication step by step:

As shown in figure 14-25;

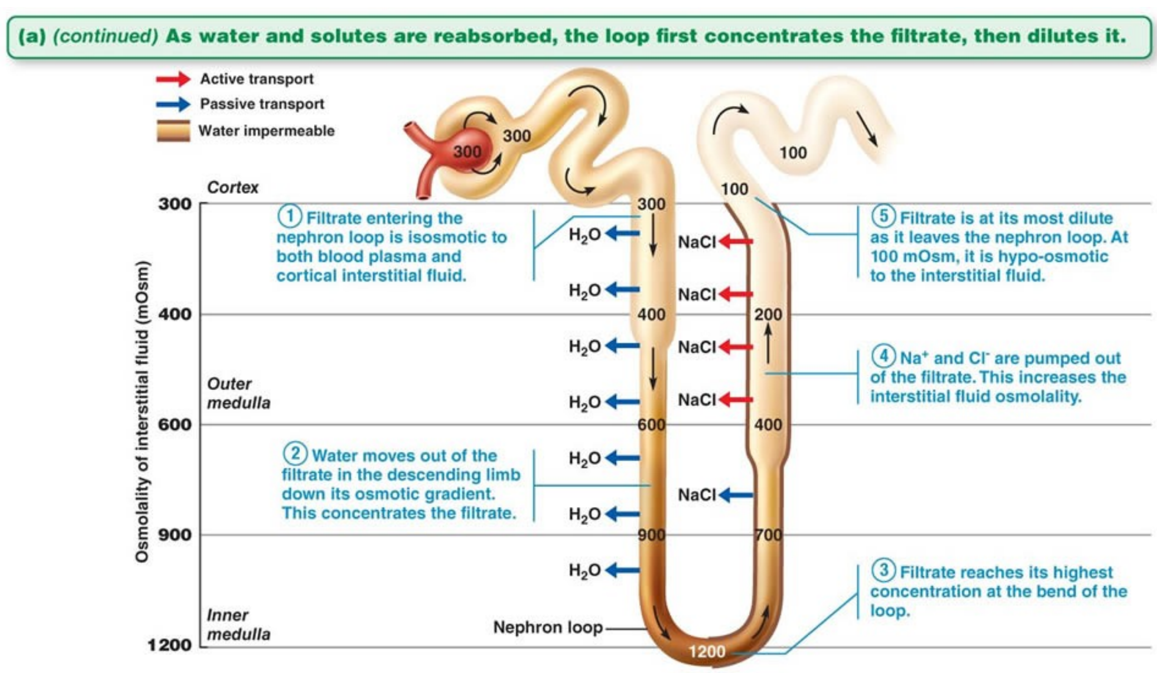
(Initial scene):

Initially, before the vertical osmotic gradient is established, the medullary interstitial fluid concentration is uniformly 300mOsm/L, as are the rest of the body fluids.

(step1):

*The active salt pump in the ascending limb can transport NaCl out of the lumen until the surrounding interstitial fluid is 200mOsm/L more concentrated than the tubular fluid in this limb.

1-The **ascending limb** *<u>pump</u>* (Na^+, K^+, $2Cl^-$ cotransport carrier protein) starts *<u>actively</u>* extruding *<u>NaCl</u>*, the medullary interstitial fluid becomes hypertonic.



2-Net diffusion of *H_2O* occurs by *osmosis* from the **descending limb** into the interstitial fluid. The *passive* movement of H_2O out of the descending limb continues until the osmolarities of the fluid in the descending limb and the interstitial fluid become equilibrated.

- Thus, the tubular fluid entering the loop of Henle immediately starts to become more concentrated as it loses H_2O. At equilibrium, the osmolarity of the ascending limb fluid is 200mOsm/L and the osmolarities of the interstitial fluid and descending limb fluid are equal at 400mOsm/L.

(step **2**):
1-As the **tubular fluid flows**, a mass of 200mOsm/L fluid exits from the top of the ascending limb into the distal tubule, and a new mass of isotonic fluid at 300mOsm/L enters the top of the descending limb from the proximal tubule.
2-At the bottom of the loop, a comparable mass of 400mOsm/L fluid from the descending limb moves forward around the tip into the ascending limb, placing it opposite a 400mOsm/L region in the descending limb, but the 200mOsm/L concentration difference has been lost at both the top and the bottom of the loop.

(step **3**):
1-The **ascending limb** pump again transports NaCl out.
2-H_2O passively leaves the **descending limb** until a 200mOsm/L difference is reestablished between the ascending limb and both the interstitial fluid and the descending limb at each horizontal level.
Note that the concentration of tubular fluid is progressively increasing in the descending limb and progressively decreasing in the ascending limb.

(step **4**):
As the **tubular fluid flows**, the 200mOsm/L concentration gradient is disrupted again at all horizontal levels.

(step5):
Again, active extrusion of NaCl from the **ascending limb**, coupled with the net diffusion of H_2O out of the **descending limb**, reestablishes the 200mOsm/L gradient at each horizontal level.

(step **6**):
As the **fluid flows** slightly forward again and ***this stepwise process continues***, the fluid in the descending limb becomes progressively more hypertonic until it reaches a maximum concentration of 1200mOsm/L at the bottom of the loop, four times the normal concentration of body fluids (300mOsm/L). Because the interstitial fluid always achieves equilibrium with the descending limb, an incremental vertical concentration gradient ranging from 300 to 1200mOsm/L is likewise established in the medullary interstitial fluid. In contrast, the concentration of the tubular fluid progressively decreases in the ascending limb as NaCl is pumped out but H_2O is unable to follow. In fact, the tubular fluid even becomes hypotonic before leaving the ascending limb to enter the distal tubule at a concentration of 100mOsm/L, one third the normal concentration of body fluids.

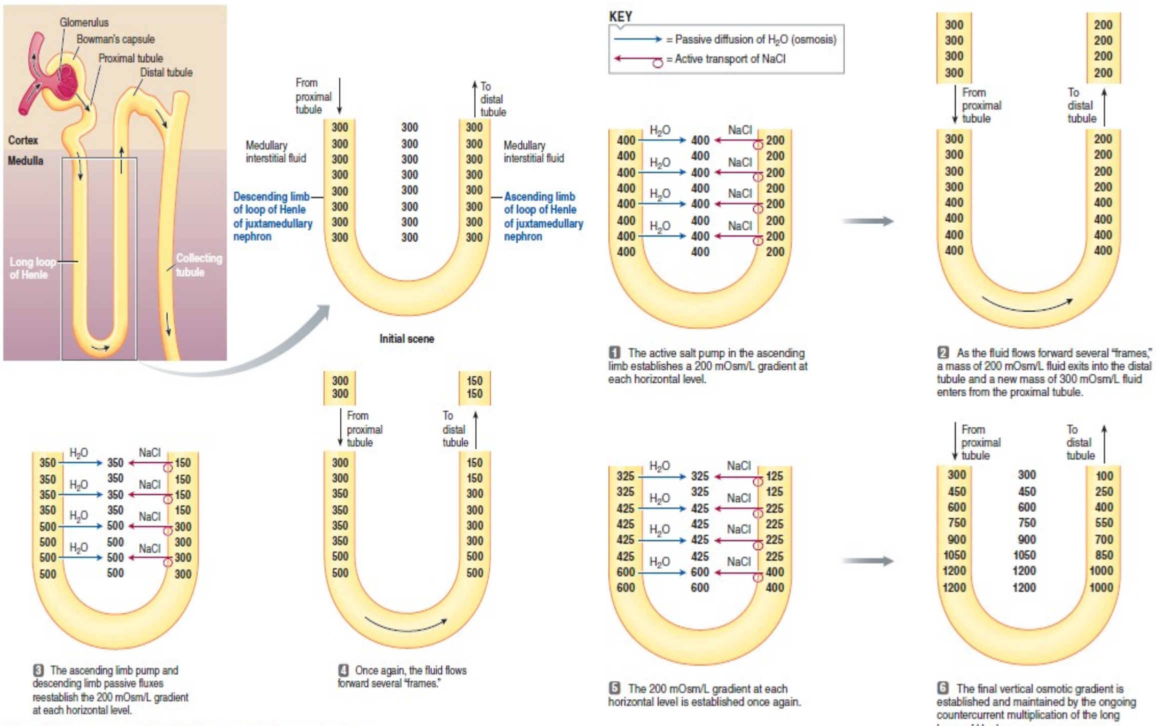


Figure 14-25 **Countercurrent multiplication in the renal medulla.** All values are in mOsm/L.

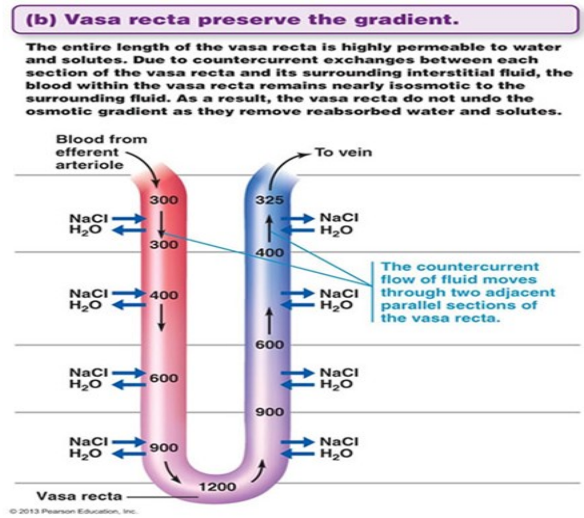
Vasa Recta
(Countercurrent exchanger)
Passive system

It is countercurrent: as the flow of blood in its descending limb is parallel, opposite, adjacent to its flow in ascending limb

It is exchanger: as it exchanges water and salts along its ascending and descending limbs

Function: Preserve the medullary interstitium hyperosmolarity.

Mechanism:



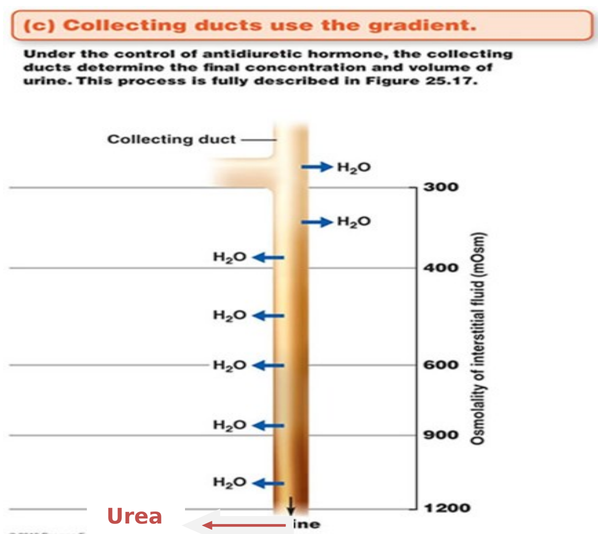
1-**Keeping salts in the interstitium**: salts diffuse passively from medullary interstitium to its descending limb gradullaly increasing its concentration inside, so in ascending limbs solutes passes out into the interstitium

2-**Removing water from the interstitium**: water comes out of its descending limb to interstitium, and then returns back to the ascending limb, then to the circulation

3- Medullary collecting duct

Function: Establishment of osmotic equilibrium between tubular fluid and medullary interstitium.

Mechanism:



-CD either cortical or medullary portions are permeable to water in presence of ADH.

-Cortical CD is impermeable to urea.

- Medullary CD is permeable to urea in presence of ADH.

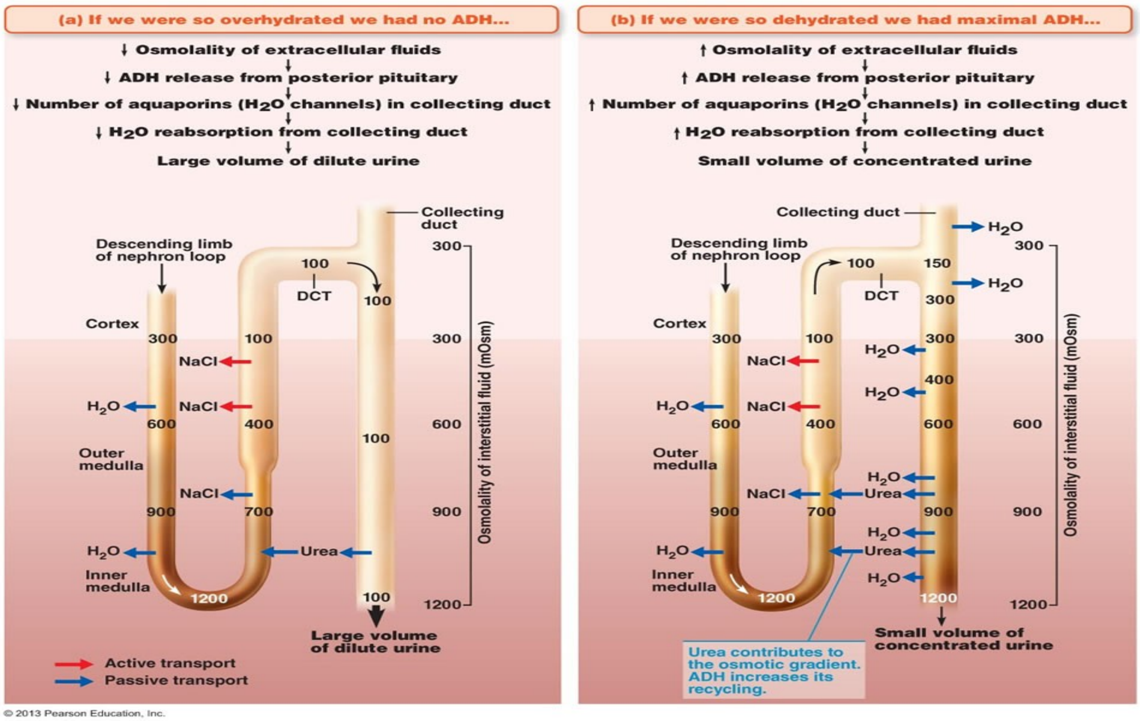
*So, by absorption of water from cortical CD, urea become concentrated in the inner medullary CD, therefore urea passes passively under concentration gradient to the interstitium, urea trapped there as the ascending limb is poorly permeable to urea.

**** Role of ADH in urine concentration:***

1- Increases the permeability of late DCT, CD (cortical, medullary portions) to **water**.
2- Increases the permeability of the inner medullary CD to **urea**.

3- Increases the activity of **Na^+-K^+- $2Cl^-$** cotransporter of thick ascending limb of LH.

4- **Vasoconstriction** of efferent arteriole of juxtamedullary nephron, decreases the blood flow in vasa recta (sluggish flow is important for urine concentration).

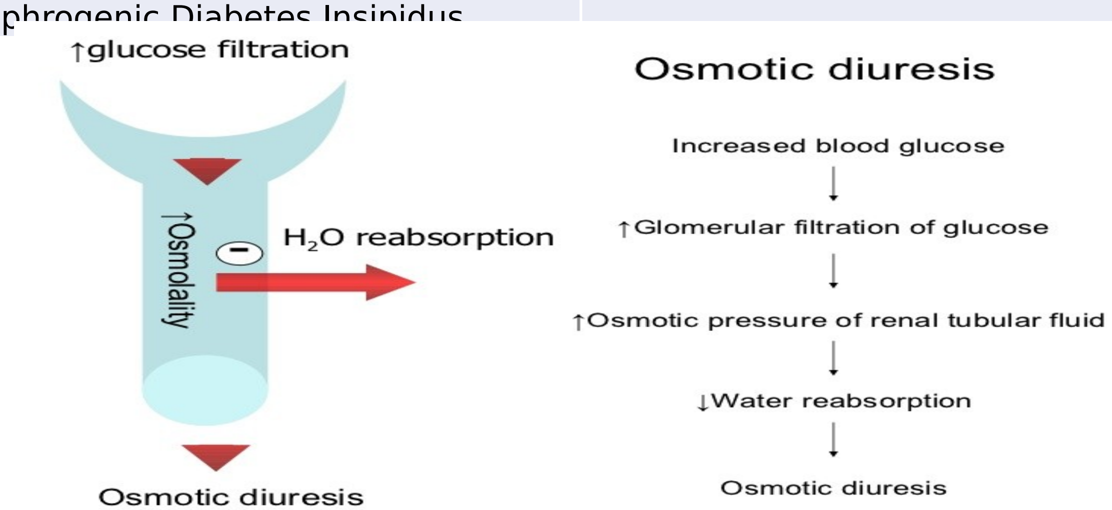


Effect of absence and presence of ADH (urine dilution and concentration):

Osmotic Diuresis

Water and Osmotic Diuresis

Water Diuresis	Osmotic Diuresis
Increased urine flow rate (no change in solute excretion) = increased pure water excretion	Increase in urine flow rate as well as increased solute excretion.
Causes: - Excess ingestion of water - Lack of ADH (neurogenic **Diabetes Insipidus**) - Defect in ADH receptors in Distal segment of nephron (nephrogenic Diabetes Insipidus)	**Causes:** - Increase plasma glucose level (**Diabetes Mellitus**) - Diuretic drugs (e.g. Lasix)
Diuresis is mainly due to decrease in water reabsorption in distal segment of nephron (affect **facultative** water reabsorption). No change to the water reabsorbed proximally	Decrease solute reabsorption results in decrease in water reabsorption proximally as well as distally (affect both **obligatory and facultative** water reabsorption)
Urine osmolality falls far below plasma osmolality.	Urine osmolality falls but remains above plasma osmolality.
Only about 20% filtered load of water reaching distal segments may remain unabsorbed and excreted in urine	Due to decreased water reabsorption in all segments of nephron, a much greater fraction of filtered water may be excreted
ADH administration will stop diuresis if it is due to lack of ADH or excess ingestion of water. ADH administration will not be effective in Nephrogenic Diabetes Insipidus	ADH administration will NOT stop diuresis.



Lecture Quiz:

Q: Complete:

-The daily obligatory H_2O reabsorption is about………

Answer: 144L/day (80% 0f filtered volume = 180 X 80/100= 144L/day)

-The daily minimum volume of obligatory H_2O loss that must accompany excretion of wastes is……….

Answer: 400 ml/ day (0.2 % of filtered volume = 180 X 0.2/100 = 360 ml/min (□ 400 ml/ day)

a. Mention requirements for urine concentration
b. Discuss role of ADH in concentrating urine

References:

Sherwood and Linda Costanzo Textbook of Medical Physiology